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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/567,950	09/08/2006	**Helen Francis-Lang**	05-967-D5	5893

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EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/567,950	FRANCIS-LANG ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11,13-15 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *4,5,7,13-15 and 20-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6 and 8-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

An amendment was received and entered on 1/29/10.

Claims 12 and 16-19 were canceled.

Claims 1-11, 13-15, and 20-25 are pending. Claims 4, 5, 7, 13-15, and 20-25 stand withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/27/09.

Claims 1-3, 6, and 8-11 are under consideration.

The PTO-Form 326 of 7/29/09 was incorrect with regard to the claims identified as pending and withdrawn. The correct claim status is set forth on the current Form 326 and above.

Rejections not reiterated are withdrawn.

Priority

This Application is the National Stage of PCT/US2004/26361, filed 8/13/2004, and claims priority to UD provisional application 60/495,172, filed 8/14/2003. The claims as currently pending are drawn to methods utilizing an assay system comprising a PRKC nucleic acid. In view of the specification as filed the term "PRKC" is taken to be synonymous with "PKC", or protein kinase C. See page 3, lines 1 and 2. Thus the claims embrace the entire genus of protein kinase C nucleic acids. The PKC family comprises a wide variety of isoforms, including alpha, $beta_I$, $beta_{II}$, delta, gamma, eta, omega, lambda, iota, and zeta. Provisional application 60/495,172 supports only PKC

zeta and PKC iota. Because the instant claims read on PKC nucleic acids that are not supported in the priority document 60/495,172, such as PKC alpha, they are not entitled to the priority date of 60/495,172. The effective filing date of the instant claims is considered to be 8/13/2004, the filing date of PCT/US2004/26361.

Drawings

The application as filed contained no drawings.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 6, 8, and 9 stand rejected under 35 U.S.C. 102(b) as being anticipated by Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993).

Murray examined the role of PKC isotypes in K562 cell proliferation and differentiation. In so doing, Murray provided a first system in which the effect of antisense against PKC isotypes was measured by northern blot. In this system, Murray contacted the cells with antisense and measured the expression of PKC isotypes in the presence and absence of the antisense, detecting a change in PKC expression (see e.g. Fig. 6 on page 15850, and page 15850, right column, lines 3-8). Thus Murray anticipated claimed method steps (a)-(d). Note that the step of "identifying a beta

catenin modulating agent" is inherent in the active steps carried out by Murray, i.e. in detecting a change in PKC expression.

Murray further provided a second assay system for determining the effect of the antisense on K562 cell proliferation. In this system K562 cells that expressed PKC alpha, $beta_{II}$, and zeta were treated with antisense against PKC $beta_{II}$. The proliferation phenotype of the cells was assayed. See abstract. Measurement of the proliferation of the cells is considered to be a measurement of the beta catenin pathway. Note that the instant specification at paragraph 11 states that changes in beta catenin pathway can be cell proliferation changes. Accordingly, measuring changes in proliferation is one way of measuring changes in the beta catenin pathway. Thus Murray anticipates steps (e)-(h), and the method as a whole.

Applicant's arguments filed 1/29/10 have been fully considered but they are not persuasive. Applicant argues that Murray did not teach steps (e)-(h), but the Office finds that Murray does teach these steps for the reasons set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 6, and 8-10 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993) in view of Summerton et al (Antisense & Nucleic acid Drug Dev. 7: 187-195, 1997).

Murray examined the role of PKC isotypes in K562 cell proliferation and differentiation. In so doing, Murray provided a first system in which the effect of antisense against PKC isotypes was measured by northern blot. In this system, Murray contacted the cells with antisense and measured the expression of PKC isotypes in the presence and absence of the antisense, detecting a change in PKC expression (see e.g. Fig. 6 on page 15850, and page 15850, right column, lines 3-8). Thus Murray anticipated claimed method steps (a)-(d). Note that the step of "identifying a beta catenin modulating agent" is inherent in the active steps carried out by Murray, i.e. in detecting a change in PKC expression. Thus Murray anticipates and renders obvious claims 1, 2, 6, 8, and 9.

Murray did not teach a PMO oligonucleotide.

Summerton taught that phosphorodiamidate morpholino (PMO) oligonucleotides overcome problems associated with first generation antisense chemistries, provide high and predictable activity in cells, and exhibit little or no nonantisense activity, afford good water solubility, are immune to nucleases. See abstract. Therefore one of ordinary skill in the art at the time of the invention would have found it obvious and would have been motivated to substitute PMO oligonucleotides for the standard oligonucleotide chemistry of Murray, in order to obtain the perceived advantages of PMO oligonucleotides.

Applicant's arguments filed 1/29/10 have been fully considered but they are not persuasive. Applicant asserts that Murray makes no mention of the beta catenin pathway, no any connection between PKC and the pathway. This is unpersuasive because Murray need not mention the pathway or its connection to PKC in order to render obvious the claims as written. The step of "identifying a beta catenin modulating agent" is inherent in the active steps carried out by Murray, i.e. in detecting a change in PKC expression, as recited in the claims. Further, the instant specification at paragraph 11 states that changes in beta catenin pathway can be cell proliferation changes. Accordingly, measuring changes in proliferation, as Murray does, is a way of measuring changes in the beta catenin pathway. Thus Murray inherently measures the beta catenin pathway in the terms set forth in the instant specification, and renders obvious steps (e)-(h) and the method as a whole.

Applicant further asserts Murray does not teach measuring PKC expression in the presence and absence of the test agent. This is incorrect. See Fig. 6 on page 15850, lanes C, P, 1-3 for PKC expression in the absence of antisense, and lane AS beta for expression in the presence of antisense.

Claims 1-3, 6, 8, 9, and 11 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Murray et al (J. Cell Biol. 145(4): 699-711, 1999) in view of Murray et al (J. Biol. Chem. 268(11): 15847-15853, 1993).

Murray (1999) taught that overexpression of PKC $beta_{II}$ induced colonic hyperproliferation and increased sensitivity to colon carcinogenesis in a transgenic

mouse model. Transgenic PKC beta$_{II}$ mice exhibited elevated colonic beta catenin levels and glycogen synthase 3beta activity indicating that PKC beta$_{II}$ stimulates the Wnt/APC/beta catenin proliferative signaling pathway in vivo.

Murray did not teach treatment of cells with antisense against PKC beta$_{II}$.

Murray (1993) studied the role of PKC beta$_{II}$ on cell proliferation in K562 erythroleukemic cells. Murray showed that proliferating cells expressed PKC beta$_{II}$, and that cells that overexpressed PKC beta$_{II}$ were less sensitive to cytostatic effects normally induced by phorbol myristate acetate (PMA). Murray also showed that proliferation of PMA-withdrawn cells can be inhibited by treatment with PKC beta$_{II}$ antisense, thereby confirming the role of PKC beta$_{II}$ in cellular proliferation. See abstract.

It would have been obvious to one of ordinary skill in the art at the time of the invention to have used the antisense of Murray (1993) to treat the colonic cells of the mouse of Murray (1999). One would have been motivated to do so, as in the case of Murray (1993), in order to confirm that the activity of PKC beta$_{II}$ in those cells was responsible for the observed phenotype (colonic hyperproliferation, increased sensitivity to colon carcinogenesis, and elevated colonic beta catenin levels and glycogen synthase 3beta activity). In so doing, one would have taken the antisense agent identified in a method anticipating the method of claims 1, 2, 6, 8, and 9 (Murray (1993)), and applied it in a second, animal-based model system in which the animal misexpressed beta catenin, and assayed cellular proliferation, thereby inherently detecting a change in the beta catenin pathway. one of ordinary skill appreciates that

such an experiment would routinely contain a control experiment in which the agent was not added, for the purpose of determining the effect of the agent. Note that the specification at paragraph 81 indicates that "defective beta catenin function" includes beta catenin overexpression or underexpression relative to wild type. So, the animal model of Murray (1999), which overexpresses beta catenin, shows defective beta catenin function as defined by the specification and required by claims 3 and 11. Thus the invention as a whole was prima facie obvious.

Applicant's arguments filed 1/29/10 have been fully considered but they are not persuasive for the reasons set forth above in the two preceding rejections.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Fereydoun Sajjadi, can be reached at (571) 272-3311. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

/Richard Schnizer/
Primary Examiner, Art Unit 1635